DE 03 TOTAL PORTING PO

1623 Wovember 30, 2004

US Patent and Trademark Office

US Department of Commerce Appn. Number: 10/007,489 Appn. Filed: 12/05/2001

Applicant: Elizabeth Gay Frayne

Title: "Microbial Production of Phosphorothioate Substituted DNA, RNA, and Oligo

Mixtures"

Examiner: Devesh Khare, PhD, JD

Art Unit:1623

RE: Office Action Summary issued Oct. 18th for Application No. 10/007,489

Dear Sir,

In response to your office action I have made the claims 1 and 5 more definite and suited to describe the active steps of the process invention. Please amend as follows:

- 1. A process for generating phosphorothioate substituted nucleic acids in vivo comprising:
 - 1) preparing microbial culture media depleted of phosphate
 - 2) adding thio-phosphate as an alternative source of phosphate to the media
 - 3) <u>culturing micro-organisms in the modified media containing thiophosphate</u>

 <u>such that thiophosphate enters into nucleotide precursor pools thereby</u>

 <u>enabling the synthesis of phosphorothioate internucleotide linkages.</u>
 - 5. The method of claim 1 where the alternative source of phosphate is a derivative of thiophosphate such as dithiophosphate or methylthiophosphate.

Note claims 2-4 should remain as previously amended.

Please under MPEP 707.07(j) the pro se applicant requests that if the Examiner fines patentable subject matter disclosed in this application, but feels that applicant's present claims are not entirely suitable, the Examiner draft one or more allowable claims for the applicant.

Respectfully submitted,

Elizabeth Lrayne

Elizabeth Frayne

Frayne Consultants

2027 Galvin Ln #1

Diamond Bar, CA

91765/ (909)860-7415